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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/823,373	03/30/2001	Sarita Chauhan	BC1032 US NA	7359

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EXAMINER	
FREDMAN, JEFFREY NORMAN	
ART UNIT	PAPER NUMBER
1637	

DATE MAILED: 04/22/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/823,373	CHAUHAN ET AL.	
	Examiner	Art Unit	
	Jeffrey Fredman	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 March 2004* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-20,24-47 and 49* is/are pending in the application.

4a) Of the above claim(s) *3,4,6-8 and 24-45* is/are withdrawn from consideration.

5)☒ Claim(s) *10,12,14,20,47 and 49* is/are allowed.

6)☒ Claim(s) *1,2,9,11,13,15-19 and 46* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) ____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Status

Claims 1-4, 6-20, 24-47 and 49 are pending.

Claims 5, 21-23, 48 are cancelled.

Claims 3, 4, 6-8 and 24-45 are withdrawn from consideration.

Claims 1, 2, 9, 11, 13, 15-19, and 46 are rejected.

Claims 10, 12, 14, 20, 47 and 49 are allowed.

Any rejection which is not reiterated in this action is hereby withdrawn as no longer applicable.

Claim Rejections - 35 USC § 112

1. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

2. Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

In analysis of the claims for compliance with the written description requirement of 35 U.S.C. 112, first paragraph, the written description guidelines note regarding genus/species situations that "Satisfactory disclosure of a ``representative number'' depends on whether one of skill in the art would recognize that the applicant was in possession of the necessary common attributes or features of the elements possessed

by the members of the genus in view of the species disclosed." (See: Federal Register: December 21, 1999 (Volume 64, Number 244), revised guidelines for written description.)

All of the current claims encompass a genus of nucleic acids which are different from those disclosed in the specification. The specification discloses several species of nitrilase enzyme sequences. However, the genus claimed includes variants for which no written description is provided in the specification. This is expressly permitted by the language of the specification and claim in which the percent homology language includes no functional requirement so that there is no common structure which must be preserved.

This large genus is represented in the specification by only the particularly named SEQ ID Nos. Thus, applicant has express possession of only two particular nitrilase sequences, in a genus which comprises hundreds of millions of different possibilities. Here, no common element or attributes of the sequences are disclosed, not even the presence of certain domains. No structural limitations or requirements which provide guidance on the identification of sequences which meet these functional limitations is provided. Further, these claims encompass alternately spliced versions of the proteins, allelic variants including insertions and mutations, inactive precursor proteins which have a removable amino terminal end, and only specific nucleic and amino acid sequences have been provided. No written description of alleles, of upstream or downstream regions containing additional sequence, or of alternative splice variants has been provided in the specification.

It is noted in the recently decided case The Regents of the University of California v. Eli Lilly and Co. 43 USPQ2d 1398 (Fed. Cir. 1997) decision by the CAFC that

> "A definition by function, as we have previously indicated, does not suffice to define the genus because it is only an indication of what the gene does, rather than what it is. See Fiers, 984 F.2d at 1169- 71, 25 USPQ2d at 1605- 06 (discussing Amgen). It is only a definition of a useful result rather than a definition of what achieves that result. Many such genes may achieve that result. The description requirement of the patent statute requires a description of an invention, not an indication of a result that one might achieve if one made that invention. See In re Wilder, 736 F.2d 1516, 1521, 222 USPQ 369, 372- 73 (Fed. Cir. 1984) (affirming rejection because the specification does "little more than outlin[e] goals appellants hope the claimed invention achieves and the problems the invention will hopefully ameliorate."). Accordingly, naming a type of material generally known to exist, in the absence of knowledge as to what that material consists of, is not a description of that material. "

In the current situation, the definition of the nitrilase gene using the hybridization language of paragraph (c) of claim 1 lack any specific required structure. Thus, these claims present precisely the situation of naming a type of material which is generally known to likely exist, but, except for the two specific nitrilase sequences given fails to provide descriptive support for these generic claims.

It is noted that in Fiers v. Sugano (25 USPQ2d, 1601), the Fed. Cir. concluded that

> "...if inventor is unable to envision detailed chemical structure of DNA sequence coding for specific protein, as well as method of obtaining it, then conception is not achieved until reduction to practice has occurred, that is, until after gene has been isolated...conception of any chemical substance, requires definition of that substance other than by its functional utility."

As already noted, the current claims define the nitrilase nucleic acids solely by their functional utility, as fragments or components capable of hybridization to specific sequences, without any definition of the particular genus of sequences claimed.

In Vas-Cath Inc. v. Mahurkar (19 USPQ2d 1111, CAFC 1991), it was concluded that:

> "...applicant must also convey, with reasonable clarity to those skilled in art, that applicant, as of filing date sought, was in possession of invention, with invention being, for purposes of "written description" inquiry, whatever is presently claimed."

In the application at the time of filing, there is no record or description which would demonstrate conception of any nucleic acids other than those expressly disclosed which encode the nitrilase enzymes disclosed. Therefore, the claims fail to meet the written description requirement by encompassing sequences which are not described in the specification.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1, 9, 11, 13 and 15 are rejected under 35 U.S.C. 102(b) as being anticipated by Kobayashi et al (Biochemistry (1992) 31:9000-9007).

Kobayashi et al teaches an isolated nucleic acid sequence fragment that encodes a nitrilase enzyme (see page 9004, figure 3) which sequence:

i) would hybridize to SEQ ID NO: 5 under the stated conditions,

ii) encompasses the completely complementary strand

iii) is 71.274 % identical to SEQ ID NO: 5 (see alignment attached to original office action).

With regard to the limitation in claim 5 that the nucleic acid be isolated from Acidovorax strain, in the absence of any structural limitations imposed by this claim limitation, this source designation is not given patentable weight. As MPEP 2111 notes "During patent examination, the pending claims must be "given the broadest reasonable interpretation consistent with the specification". Here, the broadest reasonable interpretation is that the source gives no patentable weight. As MPEP 2113 notes "If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process." Here, the only difference between the products is the claimed method of making. Since the products are the same given the scope of the claim, the products are anticipated.

Kobayashi further teaches expression of the nitrilase in an Escherichi coli host cell (see page 9001, column 1, subheading "Bacterial strains and Plasmids") which used the PUC18 vector that also comprises a Lac promoter consequently forming a chimeric gene which is operably linked to suitable regulatory sequences (see page 9001, column 1, subheading "Bacterial strains and Plasmids").

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi in view of Anderson et al (U.S. Patent 5,935,840).

Kobayashi teaches the limitations of claims 1-2, 9, 11, 13 and 15 as discussed above. Kobayashi does not teach the use of chromosomally integrated vectors or ribosome binding sites.

Anderson teaches the use of chromosomally integrated vectors and ribosome binding sites (see column 5, lines 23-38).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the expression vector of Anderson to express the

protein of Kobayashi since the use of a vector with a ribosome binding site will enhance the expression levels of the protein by more easily permitting the ribosomes to interact with the expressed mRNA and since integration of the vector will make the vector more stable and less likely to be lost from the cell, thereby enhancing efficient protein production.

8. Claim 46 is rejected under 35 U.S.C. 103(a) as being unpatentable over Kobayashi in view of Anderson et al (U.S. Patent 5,935,840) and further in view of Galen (U.S. Patent 6,413,768).

Kobayashi in view of Anderson teach the limitations of claims 16-19 as discussed above. Kobayashi in view of Anderson do not teach the specific strains listed in claim 46.

Galen teaches MG1655 (See column 33, line 19).

It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to use the cell of Galen to express the Nitrilase of Kobayashi since MPEP 2144.06 notes " Substituting equivalents known for the same purpose. In order to rely on equivalence as a rationale supporting an obviousness rejection, the equivalency must be recognized in the prior art, and cannot be based on applicant's disclosure or the mere fact that the components at issue are functional or mechanical equivalents. An express suggestion to substitute one equivalent component or process for another is not necessary to render such substitution obvious. In re Fout , 675 F.2d 297, 213 USPQ 532 (CCPA 1982)." Here, it is clear that Galen recognizes that MG1655 is a well known equivalent.

Allowable Subject Matter

9. Claims 10, 12, 14, 20, 47 and 49 are allowed.

10. The following is a statement of reasons for the indication of allowable subject matter: These claims are drawn to specific deposited plasmids in microorganisms which deposits are not taught nor suggested by the prior art. Further, it is noted that the specification complies with the deposit rules on page 5, lines 25-34. With regard to claim 47, the sequence is novel and unobvious. With regard to claim 49, the written description guidelines clearly show that 95% identity coupled with an enzymatic function meets the requirements of example 14 of the written description guidelines. Here, the 95% identity to SEQ ID NO: 5 coupled with the nitrilase activity meets this requirement.

Response to Arguments

11. Applicant's arguments filed March 4, 2004 have been fully considered but they are not persuasive.

Applicant first argues the 102 rejection. Applicant relies upon the amendment to "highly stringent" conditions for hybridization to distinguish Kobayashi from the current claims. This is not persuasive because the sequence of Kobayashi, which is 71% identical, would hybridize under "highly stringent" conditions. As noted previously, in order to anticipate the claims, Kobayashi must teach that the sequence does two things. Kobayashi must teach that the sequence encodes a nitrilase (see page 9004, figure 3). Second Kobayashi must teach a sequence which would hybridize under the conditions stated to SEQ ID NO: 5. The sequence of Kobayashi would hybridize to SEQ ID NO: 5 under the stated conditions based upon the percent identity.

Applicant correctly notes that the rejection of claim 2 is no longer applicable under Kobayashi since Kobayashi does not teach 90% identity.

Applicant relies upon overcoming Kobayashi to overcome the 103 rejections. Since Kobayashi is maintained, so are the 103 rejections.

With regard to the written description rejection, as noted above, claim 49 is no longer subject to this rejection. Claim 2, which is drawn to variants that are 90% identical, is still rejected. When the facts of the current case are compared to those of Lilly, here there is 90% homology with nitrilase function. In Lilly, there was 81% homology with insulin function, a more defined activity. The Federal Circuit found that the specification lacked possession of the corresponding human sequence of the rat insulin gene even though they shared 81% homology. The issue in the USPTO written description guidelines is whether the structure plus the function is sufficient so that there is minimal variation among the species. The guidelines indicate that 95% is sufficient (see example 14). In the current case, this expectation would not be met since the scope of the claim drawn to only 90% identity encompasses species with significant variation.

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not

mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey Fredman whose telephone number is (571)272-0742. The examiner can normally be reached on 6:30-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion can be reached on (571)272-0782. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Jeffrey Fredman
Primary Examiner
Art Unit 1637